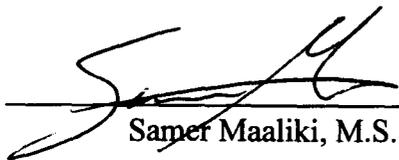


Development of a Poincaré Software to Predict Arrhythmias

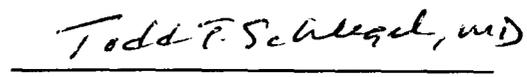
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Final Report

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Abstract

The most distressing types of heart malfunction occur because of an abnormal rhythm of the heart. Cardiac arrhythmias can be caused by abnormal rhythmicity of the pacemaker, electrolyte disturbances, blockage of the transmission of the electric impulse through the heart, and other abnormalities. There is strong evidence that space flight is associated with decreased cardiac electrical stability that may pose a life threatening risk to astronauts. For example, during the Skylab missions, a crewmember had a five beat run of ventricular tachycardia during lower body negative pressure. Also, analysis of nine 24-hour Holter monitor recordings obtained during long term spaceflight on Mir revealed one 14-beat run of ventricular tachycardia. A Mir cosmonaut was replaced in 1986 because of cardiac dysrhythmias. Most recently, in July of 1997, a Mir commander was unable to participate in the Spektr module repair due to complaints of an irregular heart rhythm. Despite these examples, possible mechanisms of arrhythmias and countermeasure strategies have barely been addressed.

The Poincaré method has been proposed as a technique that might potentially predict life-threatening arrhythmias before they occur. According to this method, each RR interval obtained from an EKG recording is plotted sequentially vs. the previous RR interval. Several studies using the method have demonstrated a strong correlation between the shape of the Poincaré plot and ventricular arrhythmia. Our purpose was to develop an automated software program that detects the "R" peaks from an EKG recording while simultaneously displaying the Poincaré plot and other related parameters.

INTRODUCTION

The pumping action of a heart is regulated by a conduction system that spreads electrical impulses from the sinoatrial node to the rest of the heart. The signal generated in the sinoatrial node first disperses through the atrial tissues causing the atria to contract. The signal then moves through the Purkinje fibers into the ventricular septum. Finally, the signal is conducted to the outer ventricular walls causing the ventricles to contract. In a normal heart, this process is very organized. However, in a diseased heart, the conduction system can be damaged. The degree of irregularity in the conduction of the impulse depends greatly on the extent and location of the disease in the heart.

Electrical potentials that originate in the heart spread out into neighboring tissues. Electrodes that are placed on the chest opposite to the heart can record these potentials. Such a recording is known as an electrocardiogram (EKG). A sample EKG is shown in Figure 1. There are three distinct peaks in an EKG signal: the P wave, the QRS complex, and the T wave. Electrical potentials, generated when the atria depolarize at the onset of atrial contraction, cause the P wave. The QRS complex is caused by potentials generated by ventricular depolarization before contraction. When the ventricle recovers from depolarization, the T wave is generated.

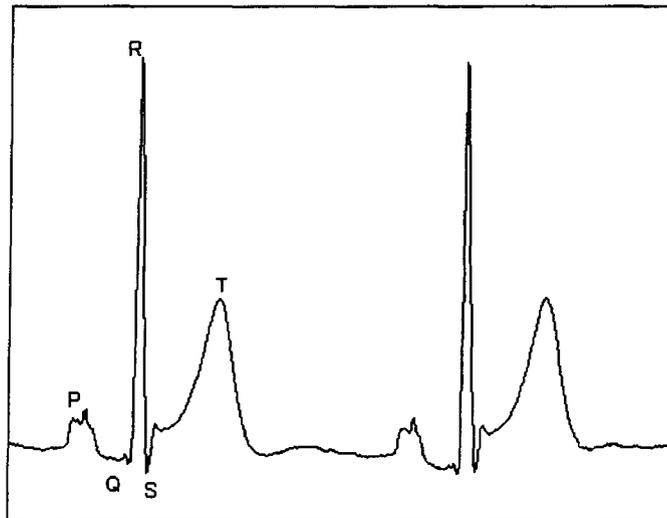


Figure 1. A Sample EKG Showing the Characteristic P, Q, R, S and T Waves.

The P-Q or P-R interval is the amount of time it takes from the onset of atrial contraction to the onset of ventricular contraction. The Q-T interval is the time of ventricular

contraction. The time between successive QRS complexes is the time it takes for a complete heart beat. This is also known as the RR interval.

By analyzing the peaks and intervals in an EKG, clinicians can determine whether the heart is functioning properly or if it is diseased. Such analysis also provides a good way of determining the type of cardiac disease that may be present. Recently, there has been an increasing interest in one method that relies on the RR interval. This method, called the Poincaré plot (2,5,12), is simply a plot of the current RR interval (RR_{n+1}) vs. the previous RR interval (RR_n). If A, B, and C are consecutive RR intervals, their Poincaré plot consists of two points with the coordinates (A,B) and (B,C). This is shown in Figure 2. When EKG recordings are of longer duration (i.e., minutes to hours), the Poincaré method provides a visual way of analyzing overall heart rate variability (HRV) (5,8). When the RR intervals are very similar, i.e., low standard deviation, the points in the Poincaré plot form a tight pattern. When the RR intervals vary a lot from beat to beat, i.e., high standard deviation, the points on the Poincaré plot are spread out. Since several studies suggest that both heart failure and impending arrhythmias can be associated with a decreased HRV (3,4,7), the Poincaré plot provides a useful diagnostic tool.

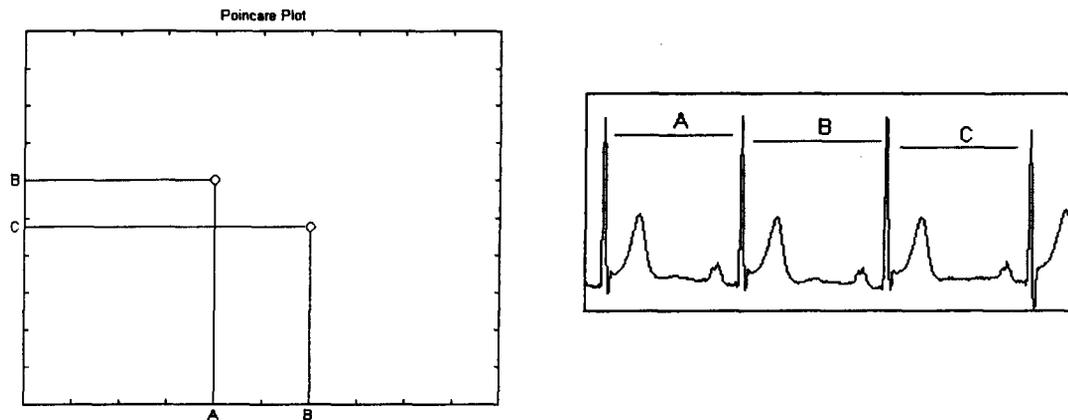


Figure 2. Poincaré Plot of Three Consecutive RR Intervals

Healthy subjects usually have a so called “comet” shaped (13) 24-hour Poincaré plot (Figure 3). The range of RR intervals is usually between 500 to 1000 ms. On the other hand, 24-hour Poincaré plots obtained from patients with heart failure may exhibit three different abnormal patterns. The most common one is the “cigar” shape. This shape is attributed to little or no increase in R-R variability at lower heart rates. The second Poincaré plot pattern from unhealthy subjects is the “fan” shape. Both of the cigar and fan patterns have a much lower RR interval range. The third pattern is a “complex” pattern that is a combination of the cigar and fan patterns that are spread out over the entire plot.

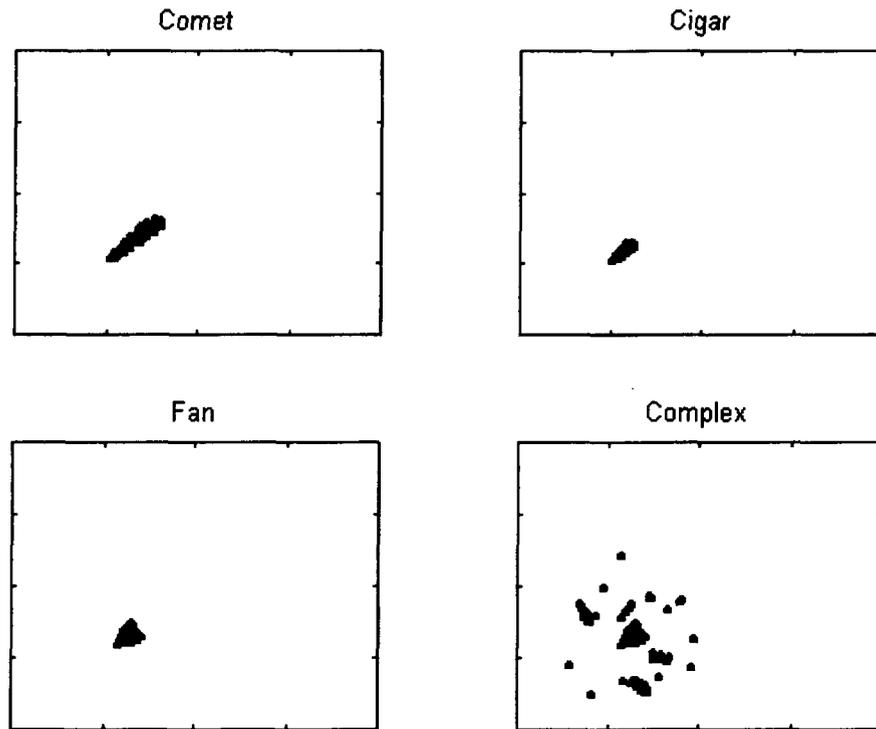


Figure 3. Different Patterns of a 24-hour Poincaré Plot.

METHODS

The first step in generating a Poincaré plot is to acquire the locations of the R-peaks in the signal. To accomplish this goal, an R-wave detector was developed that functions as follows: First, the Fast Fourier Transform (FFT) of the EKG signal is determined. Next, the lower frequencies of the Fourier spectrum are filtered out. Figure 4 shows the Fourier spectrum of an EKG signal before and after filtering. By filtering the spectrum, the slower components of the EKG signal are removed. Finally, the Inverse Fast Fourier Transform (IFFT) is computed from the filtered spectrum, and a modified version of the EKG signal is obtained. The only significant peaks in this modified signal are the R waves (Figure 5).

The locations of the R peaks were determined using a custom made peak detector. This detector first divides the signal up into different windows. For each window it then computes the maximum. Finally, the detector scans through the maxima to determine which windows have a maximum that has a higher value than the two maxima in the

surrounding windows. The location of that maximum in the EKG signal is then determined and saved as an R peak.

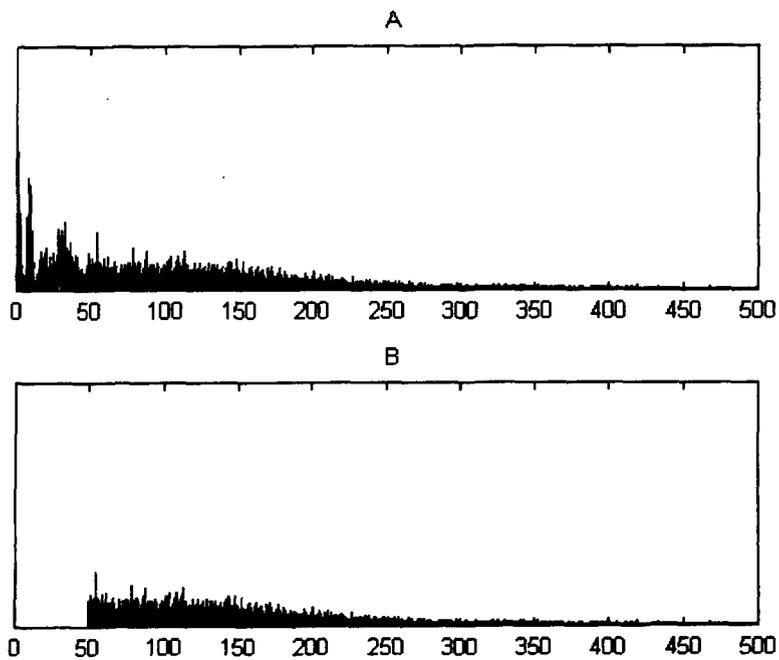


Figure 4. (A) FFT of EKG Signal Before Filtering. (B) FFT After Filtering.

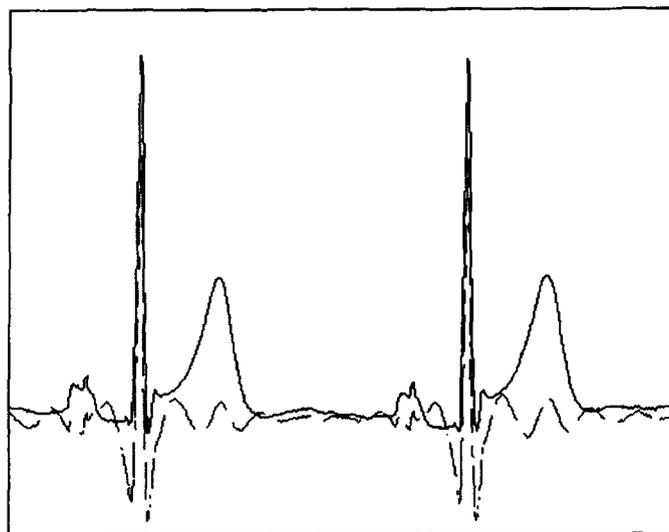


Figure 5. The EKG Signal Before (solid) and After (dashed) Filtering.

From the locations of the R peaks, the RR intervals can then be calculated. Most of the important information regarding HRV can be obtained from the RR intervals. The following is a short list of some of these variables and their descriptions (9).

RRmean	Average of RR intervals
RRstd	Standard deviation of RR intervals
ΔRR	Difference between elements of RR_{n+1} and RR_n
ΔRRstd	Standard deviation of Δ RR
RR_nstd	Standard deviation of RR_n
RR_{n+1}std	Standard deviation of RR_{n+1}
nRR_nstd	RR_n std / RRstd
nRR_{n+1}std	RR_{n+1} std / RRstd
NN50	Sum of elements of Δ RR that are less than 50 ms
pNN50	NN50 divided by length of Δ RR

By plotting RR_{n+1} vs. RR_n , a Poincaré plot is generated. Once the Poincaré plot is acquired, an ellipse (3) is fitted to the data (Figure 6). To produce such an ellipse, the confidence interval method was used. Knowing the means (μ_1, μ_2), standard deviations (σ_1, σ_2) and the correlation coefficient (ρ) of RR_n and RR_{n+1} , one can define an ellipse that encloses a desired percentage of the data. The equation for such an ellipse is the following:

$$\frac{1}{2(1-\rho^2)} \left(\frac{(x-\mu_1)^2}{\sigma_1^2} - \frac{2\rho(x-\mu_1)(y-\mu_2)}{\sigma_1\sigma_2} + \frac{(y-\mu_2)^2}{\sigma_2^2} \right) = -\log\left(\frac{n}{100}\right), \quad \text{Eq. 1}$$

where n is the desired percentage of data to be enclosed within the ellipse. In Equation 1, one can assume that RR_n and RR_{n+1} have the same mean ($\mu_1 = \mu_2 = \mu$) and standard deviations ($\sigma_1 = \sigma_2 = \sigma$), which simplifies the equation into the following:

$$\frac{1}{2\sigma^2(1-\rho^2)} \left((x-\mu)^2 - 2\rho(x-\mu)(y-\mu) + (y-\mu)^2 \right) = -\log\left(\frac{n}{100}\right). \quad \text{Eq. 2}$$

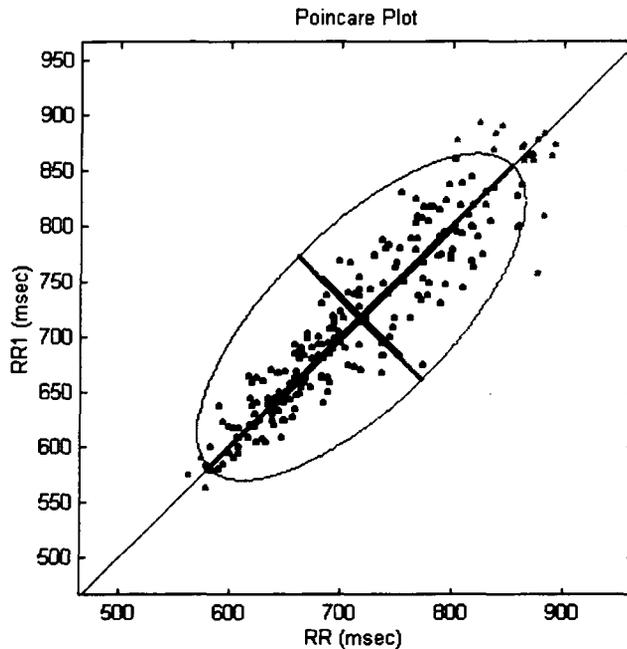


Figure 6. A Poincaré Plot with its Ellipse and Axes.

The only variables in this equation are x and y . Therefore, by substituting for either of these variables, the other variable can be determined. Using x and y the ellipse can be superimposed on the Poincaré plot. The major and minor axes of the ellipse can then be determined. These axes are directly proportional to $RR_n\text{std}$ and $RR_{n+1}\text{std}$, respectively.

The histograms of RR and ΔRR can also be determined (Figure 7). These histograms are then analyzed to calculate the HRV triangular index and the triangular index of RR (TIRR) (7). The HRV triangular index is defined as the number of RR intervals divided by the maximum of the RR histogram. TIRR is the base (B) of the triangle fit to the histogram. To find B , the area under the histogram is first computed. The area of a triangle is the product of B and the height (H), divided by 2. If H is equal to the maximum of the histogram, then B can be calculated from the area of the triangle. To plot the triangular fit, the ratio of the area of the histogram before the maximum to the area of the histogram after the maximum is first calculated. The base is then positioned so that the ratio of its length before the maximum to its length after the maximum is equal to the ratio of the areas.

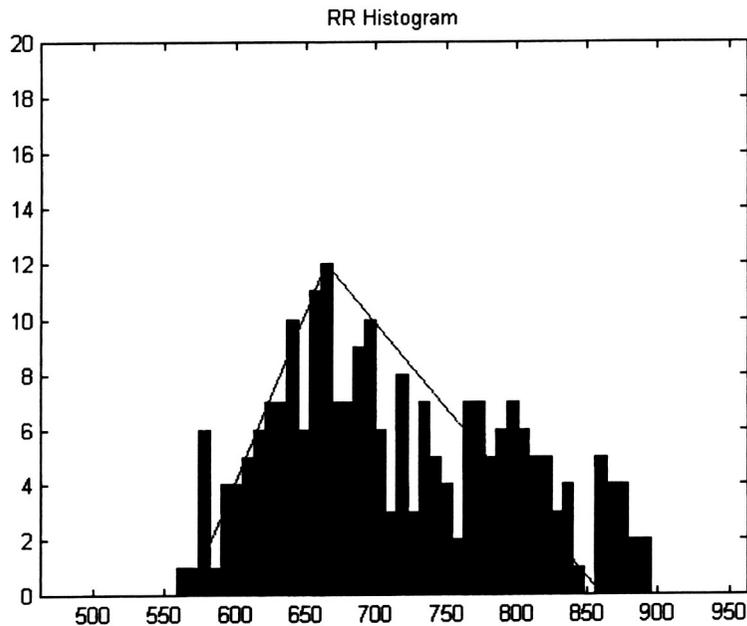


Figure 7. RR Histogram Showing the Triangular Fit.

RESULTS

Software Package

To carry out these methods and calculations in an automatic and easy manner, a graphical user interface package was developed using Matlab. This package allows the user to open several formats of EKG signals. The electrocardiogram is immediately displayed when the data file is successfully opened. The user can then analyze the data using several options in the package. The first option is detecting the R peaks in the signal. When this method is called from the menu, a window like that shown in Figure 8, is opened. In this window, there is a plot of the EKG signal with the R-wave peaks marked by asterisks, a slider to scroll through the signal, an edit box to change the size of the window used to detect the R peak, and a [Recalculate] button that recalculates the peaks according to the window size that is defined in the edit box.

The second option in this package is the Poincaré analysis. When this menu item is chosen, the Poincaré plot is displayed along with the ellipse that fits a default percentage of data. This plot also shows the major and minor axes. The third option is to plot the histograms of RR and ΔRR .

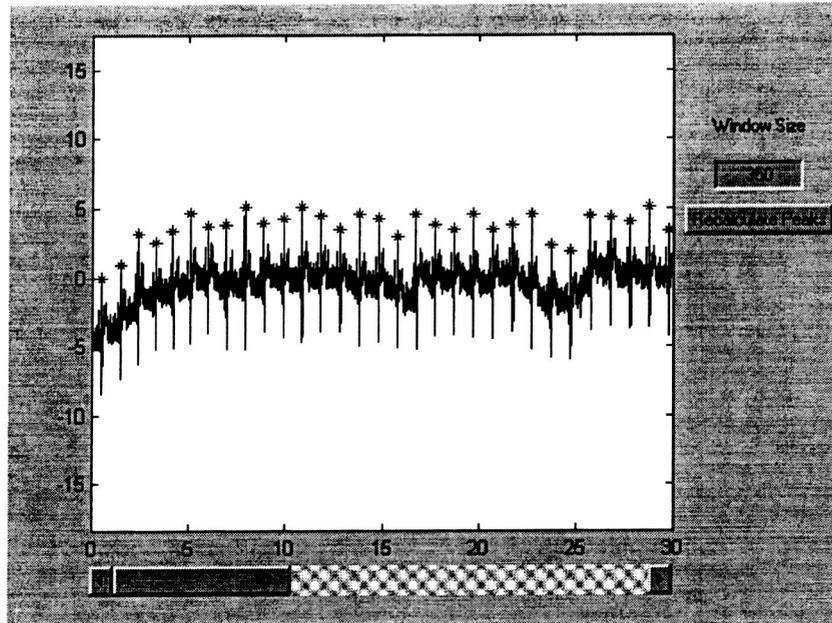


Figure 8. The R Detector Window

It is also possible to generate a 3D Poincaré plot (10,11). In such a plot (Figure 9), each point's coordinates are $(RR_{n+2}, RR_{n+1}, RR_n)$. Once the analysis is finished, the user can print out a list of all the variables associated with the methods described in this paper.

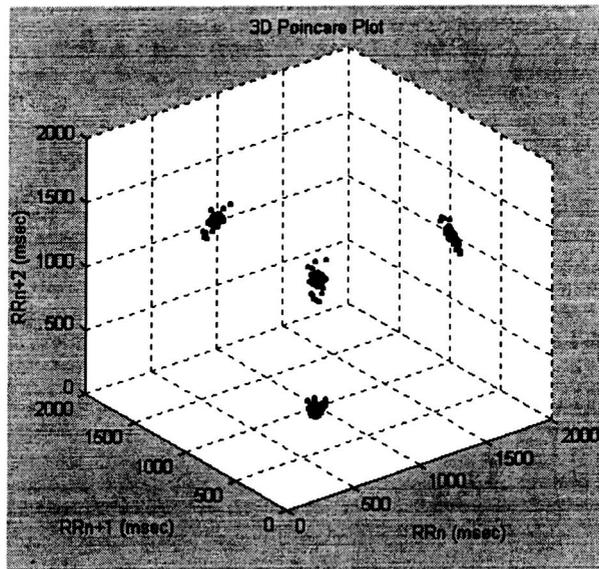


Figure 9. 3D Poincaré Plot Example

Data Analysis

Two EKG signals obtained from a healthy and non-healthy subject were analyzed to obtain the Poincaré plots shown in Figure 10. There is a remarkable difference between the healthy subject's Poincaré plot and that of the unhealthy subject. This shows that the methods integrated into this software provide reliable data.

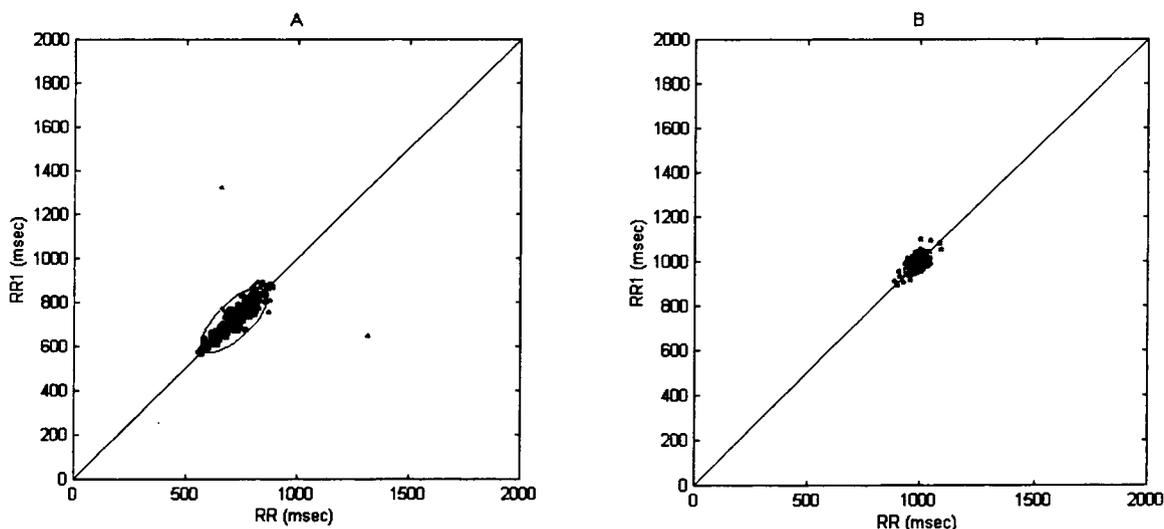


Figure 10. Poincaré Plots From a (A) Healthy Subject and a Subject with Heart Disease

CONCLUSION

In this project, the Poincaré method of analyzing HRV was automated. The software package that was developed allows the user to open an EKG file and process the data to obtain a Poincaré plot, histograms of RR intervals, and variables that can help physicians determine whether the patient's heart is functioning normally or abnormally.

The Poincaré package developed in this project can only be used in a Matlab compiler. Therefore, for further research, the methods involved in this package should be integrated into a standalone software package. The R wave detector is also a very rudimentary one. A more sophisticated R wave detector where no user input is needed would automate the software even further. Also, this package works offline only. It would be a greater asset for physicians to be able to monitor the Poincaré plot in real time.

Several other analysis tools can be added to this package to enhance its diagnostic use. The approximate entropy (ApEn) method (1,6) for assessing complexity of the EKG

signal provides a sensitive marker for changes in HRV. The power spectral density (PSD) of RR intervals can also be added to this package. PSD (2,9) is used to study the sympathetic and parasympathetic neural control to the heart.

REFERENCES

1. Goldberger, A. L., J E. Meitus, D. R. Rigney, M. L. Wood and S. M. Fortney "Effects of head-down bed rest on complex heart rate variability: response to LBNP testing." *J. Appl. Physiol.* 1994; 77(6): 2863-2869.
2. Hayano, J., H. Takahashi, T. Toriyama, S. Mukai, A. Okada, S. Sakata, A. Yamada, N. Ohte and H. Kawahara "Prognostic value of heart rate variability during long-term follow-up in chronic haemodialysis patients with end-stage renal disease." *Nephrol. Dial. Transplant.* 1999; 14(6): 1480-1488.
3. Huikuri, H. V., T. S. Seppänen, M. J. Koistinen, K.E. Juhani Airaksinen, M.J. Ikäheimo, A. Castellanos and R. J. Myerburg "Abnormalities in beat-to-beat dynamics of heart rate before the spontaneous onset of life-threatening ventricular tachyarrhythmias in patients with prior myocardial infarction." *Circulation* 1996; 93: 1836-1844.
4. Kamen, P. W. and A. M. Tonkin "Application of the Poincaré plot to heart rate variability: a new measure of functional status in heart failure." *Aust. NZ J. Med.* 1995; 25: 18-26.
5. Kamen, P. W., H. Krum and A. M. Tonkin "Poincare plot of heart rate variability allows quantitative display of parasympathetic nervous activity in humans." *Clinical Science* 1996; 91: 201-208.
6. Kaplan, D. T., M. I. Furman, S. M. Pincus, S. M. Ryan, L. A. Lipsitz, and A. L. Goldberger "Aging and the complexity of cardiovascular dynamics." *Biophys. J.* 1991; 59: 945-949.
7. Malik, Marek "Heart rate variability: standards of measurement, physiological interpretation, and clinical use." *Eur. Heart J.* 1996; 17: 354-381.
8. Otzenberger, H., C. Gronfier, C. Simon, A. Charloux, J. Ehrhart, F. Piquard and G. Brandenberger "Dynamic heart rate variability: a tool for exploring sympathovagal balance continuously during sleep in men." *Am. J. Physiol.* 1998; 275: H946-H950.
9. Pieper, S. J. and S. C. Hammill "Heart rate variability: Technique and investigational applications in cardiovascular medicine." *Mayo Clin. Proc.* 1995; 70: 955-964.
10. Schmidt, G. and G. E. Morfill "Complexity diagnostics in cardiology: Fundamental considerations." *PACE* 1994; 17: 1174-1177.

11. Schmidt, G. and G. E. Morfill "Complexity diagnostics in cardiology: Methods." *PACE* 1994; 17: 2336-2341.
12. Woo, M. A., W. G. Stevenson, D. K. Moser, H. R. Middlekauff "Complex heart rate variability and serum norepinephrine levels in patients with advanced heart failure." *J. Am. Coll. Cardiol.* 1994; 23: 565-569.
13. Woo, M. A., W. G. Stevenson, D. K. Moser, R. B. Trelease and R. M. Harper "Patterns of beat-to-beat heart rate variability in advanced heart failure." *Am. Heart J.* 1992; 123: 704-710.